REMARKS

The present invention is directed to a novel class of compounds and their use in treating disorders in which elevated PARP activities occur.

The Examiner has rejected claims 1-26 under 35 U.S.C. §112, first paragraph as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner objected to R^2 representing NR^{22} R^{23} in claims 1 and 2, R^2 representing OH in claim 1 and the definition of K in claim 1.

The Examiner has also rejected claims 1-26 under 35 U.S.C. §112, second paragraph, as indefinite. Specifically, the Examiner has objected to the definition of K in claim 1 and to the lack of antecedent basis for several substituents in claims 2, 3, 7 and 8.

Applicants have amended several of the claims in an effort to address the Examiner's objections and also offer the following remarks.

With respect to the definitions of R^2 representing NR^{22} R^{23} and OH in claim 1, an obvious typographical error (the omission of a comma between NR^{22} R^{23} and OH) has been corrected. This is consistent with the observation by the Examiner in the first Office Action that NR^{22} R^{23}OH has the wrong number of valences and the definition of R^2 in claim 6 where R^2 is NH_2. R^2 can only be NH_2 if R^2 in claim 1 is NR^{22} R^{23} where R^{22} and R^{23} are both hydrogen. Thus, it is submitted that this change is only the correction of a typographical error and not new matter.

Applicants have amended the definition of K in claim 1 to conform to the original wording of the originally filed claims. Thus, this objection should no longer apply.

With respect to claim 2, the Examiner has objected to R^4 being OR^{41}. R^{41} represents a hydrogen or C_1-C_4 alkyl group. Thus, the hydroxyl group and the O-C_1-C_4 alkyl group, in the definition of R^4 in claim 1, have been combined as the substituent OR^{41} in claim 2 and there is an antecedent basis in claim 1 for this definition.

Similarly, R^3 is defined as being $-O-(CH_2)_o-(CHR^{31})_m-(CH_2)_n-G$ with R^{31} being hydrogen, C_1-C_4 alkyl, OH and O- C_1-C_4 alkyl. This formula can be derived from the definition of R^3 in claim 1 from the formula representing the carbon chains defining the substituents F^1 and F^2 in claim 1. O in claim 2 represents the variable D in claim 1 and q in claim 1 is zero in the formula of claim 2. The maximum number of carbon atoms in a chain in claim 2 does not exceed 8, whereas claim 1 permits a maximum of 16 carbon atoms in a chain.

The variable R^{31} in claim 2 represents the substitution pattern of the carbon chain in the variables F^1 and F^2 in claim 1. Applicants have deleted R^{31} as C_1-C_4 alkyl to conform R^3 in claim 2 to R^3 in claim 1.

Applicants have amended claim 3 to be consistent with claim 1. In claim 3, R^3 represents three different heterocycles. The pyrole and imidazole derivatives are directly derived from the definition of R^3 in claim 1 from the general formula $-E-(D)_u-(F^2)_s-(G)_v$ with u being zero, v being 1, E being a pyrole or imidazole ring and F^2 being $-(CH_2)_o-(CHR^{31})_m-(CH_2)_n-$, which corresponds to the definition of R^{32} in claim 3. Claim 3 has also been amended to delete CHO from the definition of R^{32}.

With regard to the last heterocycle in the definition of R^3 in claim 3, the formula shows a combination of a 6-membered and a 7-membered nitrogen containing ring which is provided for in the variable B of claim 1.

The same arguments apply to the definition of R^{32} in claim 7. Furthermore, applicants have amended claim 7 in an effort to eliminate any inconsistencies between claim 7 and claim 1.

Claim 8 has been amended to be consistent with claim 1.

Applicants have also added the substituent –CO-NHR^{53} to the definition of R^{52} in claim 1. This substituent was inadvertently omitted from the application as filed but was present in the PCT priority application (see attached page 57 from PCT/EP99/08169).

Applicants have also amended claims 3 and 7 in order to remove other inconsistencies from these claims.

It is submitted that claims 1-26, as presently amended, comply with the requirements of 35 U.S.C. §112, first and second paragraphs. Withdrawal of these rejections is respectfully requested.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account number 23-0785.

Respectfully submitted,

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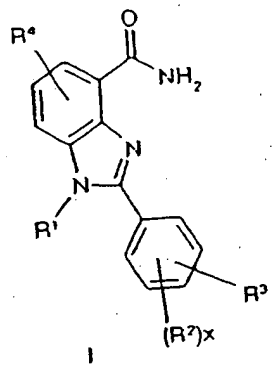
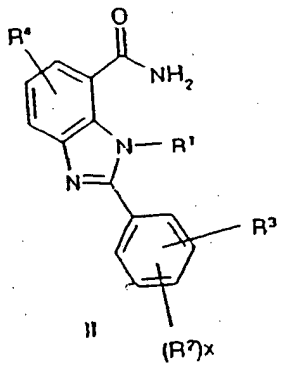
Marked-Up Version of Claims

1. (amended) A compound of the formula I or II



I



II

in which

R^1 is hydrogen, or branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, $NHCOR^{21}$, $NR^{22}R^{23}$, OH, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, CN, a straight or branched C_1 - C_6-alkyl, OR^{21} or phenyl, it also being possible for the phenyl rings to be substituted by at most two radicals R^{24}, and R^{21} and R^{22} independently of one another are hydrogen or C_1-C_4-alkyl and R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and R^{24} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro or NH_2, and

x may be 0, 1 or 2 and

R^3 is -D-$(F^1)_p$-$(E)_q$-$(F^2)_r$ -G, where p, q and r may not simultaneously be 0, or is -E-$(D)_u$-$(F^2)_s$-$(G)_v$, it also being possible for the radical E to be substituted by one or two radicals A, and if v = 0, E is imidazole, pyrrole, pyridine, pyrimidine, piperazine, pyrazine, pyrrolidine or piperidine, or R^3 is B and

R^4 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, OH, nitro, CF_3, CN, $NR^{41}R^{42}$, NH-CO-R^{43}, or O-C_1-C_4-alkyl, where R^{41} and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl

and R^{43} is hydrogen, C_1-C_4-alkyl, C_1-C_4-alkylphenyl or phenyl, and

D is S or O

E is phenyl, imidazole, pyrrole, thiophene, pyridine, pyrimidine, piperazine, pyrazine, furan, thiazole, isoxazole, pyrrolidine, piperidine, or trihydroazepine and

F^1 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or O-C_1-C_4-alkyl group and

F^2 is a chain of 1 to 8 carbon atoms, it also being possible for one carbon atom of the chain to carry an OH or O-C_1-C_4-alkyl group and

p may be 0 or 1

q may be 0 or 1, and

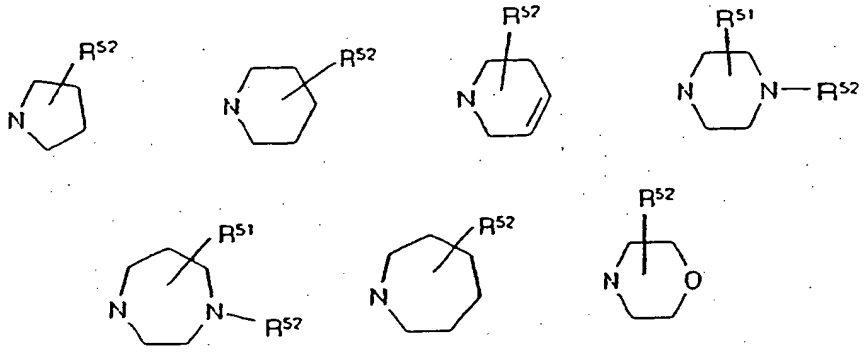
r may be 0 or 1 and

s may be 0 or 1

u may be 0 or 1

v may be 0 or 1

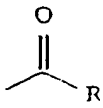
G may be $NR^{51}R^{52}$ or



and

R^{51} is hydrogen or branched and unbranched C_1-C_6-alkyl, or $(CH_2)_t$-K and

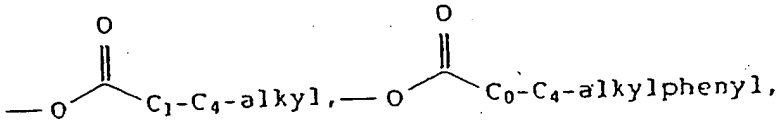
R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl, phenyl,

 , $-SO_2R^{53}$, $-(C=N)-R^{53}$, $-(C=N)-NHR^{53}$, $-CO-NHR^{53}$

in which

R^{53} may be branched or unbranched O-C_1-C_6-alkyl, phenyl, or branched or unbranched C_1-C_4-alkylphenyl, where in the case of R^{52} and R^{53}, independently of one another, one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl, it also being possible for the carbocycles of the radicals R^{52} and R^{53} independently of one another to carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl,

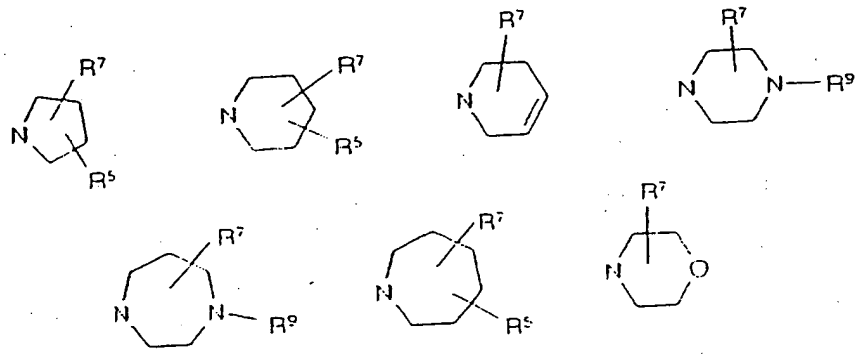
OH, F, Cl, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, CCl_3, C_1-C_4-dialkylamino, SO_2-C_1-C_4- alkyl, SO_2phenyl, $CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkylphenyl, $NHSO_2$-C_1-C_4-alkyl, $NHSO_2$phenyl, S-C_1-C_4-alkyl,



CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkylphenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkylphenyl, -SO_2NH_2, -SO_2NH- C_1-C_4-alkyl

or two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

B may be



and

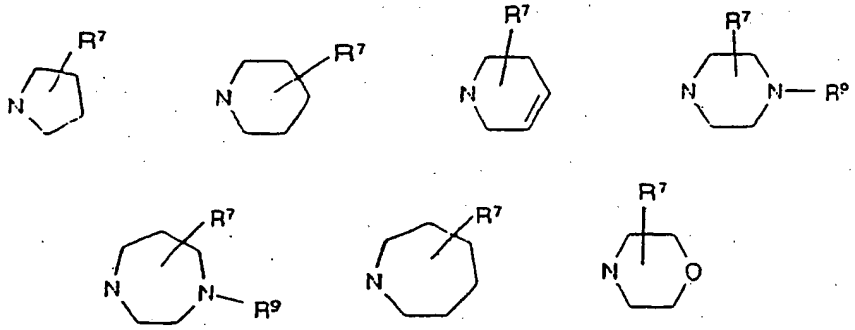
A may be hydrogen, chlorine, bromine, iodine, fluorine, CF_3, nitro, OH, O-C_1-C_4-alkyl, O-C_1-C_4-alkylphenyl, NH_2, branched and unbranched C_1-C_6-alkyl, CN, or NH-CO-R^{33}, where R^{33} is hydrogen, C_1-C_4-alkyl or phenyl and

t is 0,1,2,3, or 4 and

K is a phenyl [optionally having] which may carry at most two [substituents on the ring, Rk1 and/or Rk2 are any of the radicals defined for R41 and R42, respectively, or] radicals R, is $NR^{k1}R^{k2}$ where R^{k1} and R^{k2} are as defined for R^{41} and R^{42} respectively, NH-C_1-C_4-alkylphenyl, pyrrolidine, piperidine, 1, 2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

C_4-alkylphenyl, pyrrolidine, piperidine, 1,2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

R^5 may be hydrogen, C_1-C_6-alkyl, or NR^7R^9 and



and

R^7 is hydrogen, C_1-C_6-alkyl, C_1-C_4-alkylphenyl, or phenyl, it also being possible for the rings to be substituted by up to two radicals R^{71}, and

R^{71} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3, nitro, or NH_2, and

R^8 is hydrogen, C_1-C_6-alkyl, phenyl, or C_1-C_4-alkylphenyl, it also being possible for the ring to be substituted by up to two radicals R^{81}, and

R^{81} is OH, C_1-C_6-alkyl, O-C_1-C_4-alkyl, chlorine, bromine, iodine, fluorine, CF_3,

nitro, or NH_2 and

R^9 is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one or two hydrogens of the C_1-C_6-alkyl radical to be substituted in each case by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and for the phenyl ring also to carry one or two of the following radicals: iodine, chlorine, bromine, fluorine, branched and unbranched C_1-C_6-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C4-alkyl, CN, CF_3, or SO_2-C_1-C_4-alkyl,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

Please amend claim 2 as follows:

2. (amended). A compound of the formula I or II as claimed in claim 1 in which

R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{22}R^{23}$, NH-CO-R^{21}, OR^{21}, where

R^{21} and R^{22} are, independently of one another, hydrogen or C_1-C_4-alkyl, and

R^{23} is hydrogen, C_1-C_4-alkyl or phenyl, and

R^3 is -O-$(CH_2)_o$-$(CHR^{31})_m$-$(CH_2)_n$-G, where

R^{31} is hydrogen, [C_1-C_4-alkyl,] OH and O-C_1-C_4-alkyl,

m,o are, independently of one another, 0, 1 or 2, and

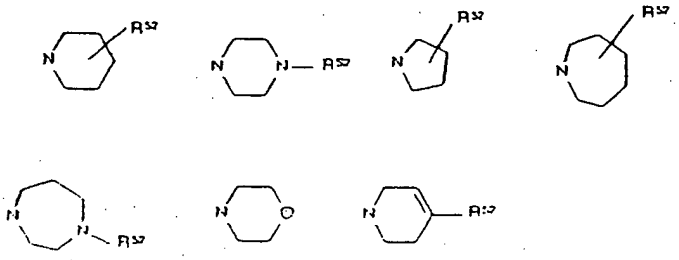
n is 1, 2, 3 or 4 and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$, NH-CO-R^{43}, OR^{41} where

R^{41} and R^{42} are, independently of one another, hydrogen or C_1-C_4-alkyl, and

R^{43} is C_1-C_4-alkyl or phenyl, and

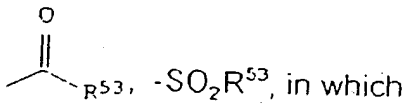
G is $NR^{51}R^{52}$ or one of the following radicals



where

R^{51} is hydrogen and branched and unbranched C_1-C_6-alkyl, and

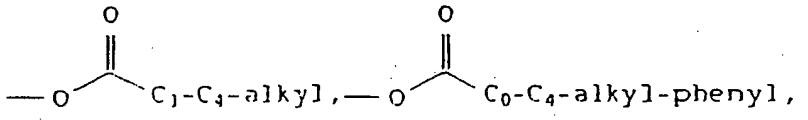
R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl phenyl,



, $-SO_2R^{53}$, in which

R^{53} is branched or unbranched O-C_1-C_6-alkyl, phenyl, branched or unbranched C_1-C_4-alkyl-phenyl, where one hydrogen in the C_1-C_6-alkyl radical in R^{52} and R^{53} are, independently of one another, optionally substituted by one of the following radicals: OH, O-C_1-C_4-alkyl, cyclohexyl, cyclopentyl, tetrahydronaphthyl, cyclopropyl, cyclobutyl, cycloheptyl, naphthyl and phenyl,

where the carbocycles of the R^{52} and R^{53} radicals may also, independently of one another, carry one or two of the following radicals: branched or unbranched C_1-C_6-alkyl, branched or unbranched O-C_1-C_4-alkyl, OH, F, Cl, Br, I, CF_3, NO_2, NH_2, CN, COOH, $COOC_1$-C_4-alkyl, C_1-C_4-alkylamino, CCl_3, C_1-C_4-dialkylamino, SO_2-C_1-C_4-alkyl, SO_2phenyl, $CONH_2$, CONH-C_1-C_4-alkyl, CONHphenyl, CONH-C_1-C_4-alkyl-phenyl, $NHSO_2$-C_1-C_4-alkyl, $NHSO_2$phenyl, S-C_1-C_4-alkyl,



CHO, CH_2-O-C_1-C_4-alkyl, -CH_2O-C_1-C_4-alkyl-phenyl, -CH_2OH, -SO-C_1-C_4-alkyl, -SO-C_1-C_4-alkyl-phenyl, SO_2NH_2, -SO_2NH-C_1-C_4-alkyl and two radicals form a bridge -O-$(CH_2)_{1,2}$-O-,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

Please amend claim 3 as follows:

3. (amended). A compound of the formula I or II as claimed in claim 1 in which

R^1 is hydrogen, branched and unbranched C_1-C_6-alkyl, it also being possible for one C atom of the alkyl radical to carry OR^{11} or a group R^5, where

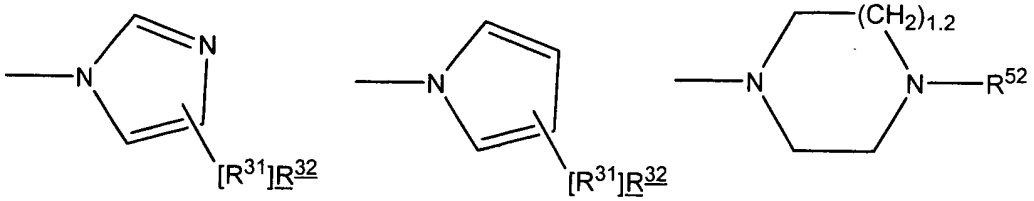
R^{11} is hydrogen or C_1-C_4-alkyl, and

R^2 is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1-C_6-alkyl, nitro, CF_3, CN, $NR^{22}R^{23}$, NH-CO-R^{21}, OR^{21}, where

R^{21} and R^{22} independently of one another are hydrogen or C_1-C_4-alkyl and

R^{23} is hydrogen, C_1-C_4 alkyl or phenyl

R^3 is



and

$[R^{31}]\,R^{32}$ is hydrogen [,CHO] and $[-(CH_2)_o-(CHR^{32})_m-(CH_2)_n-G\,]-(CH_2)_o-(CHR^{31})_m-(CH_2)_n-G$ where $[R^{32}]\,R^{31}$ is hydrogen,

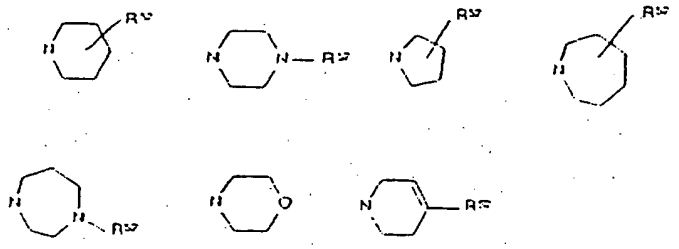
1 or 2 and n is 1, 2, 3 or 4, and

R^4 is hydrogen, branched and unbranched C_1-C_6-alkyl, chlorine, bromine, fluorine, nitro, cyano, $NR^{41}R^{42}$, NH-CO-R^{43}, OR^{41}, where

$R^{41}$and R^{42} independently of one another are hydrogen or C_1-C_4-alkyl and

R^{43} is C_1-C_4-alkyl or phenyl, and

G is $NR^{51}R^{52}$ or one of the radicals below



where

R^{51} is hydrogen and branched and unbranched and C_1-C_6-alkyl and

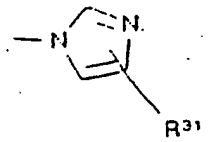
R^{52} is hydrogen, $COCH_3$, CO-O-C_1-C_4-alkyl, $COCF_3$, branched and unbranched C_1-C_6-alkyl, it being possible for one hydrogen of the C_1-C_6-alkyl radical to be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl and for the phenyl ring also to carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl, nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl,

or a tautomeric form, a possible enantiomeric or disasteriomeric form, a prodrug or pharmacologically tolerated salt thereof.

Please amend claim 7 as follows:

7. (amended). A compound as claimed in claim 1 where

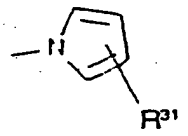
(i) for R^3 being



R^{31} is hydrogen or [–$(CH_2)_p$-G] –$(CH_2)_w$-F, where

[p] w is 1 or 2 and

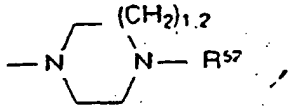
(ii) for R^3 being



R^{31} is hydrogen or $-(CH_2)_p$-G, where

p is 1 or 2 and

and (iii) for R^3 being

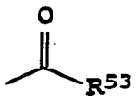


where R^{52} is hydrogen, branched and unbranched C_1-C_6-alkyl, where one hydrogen of the C_1-C_6-alkyl radical may be substituted by one of the following radicals: OH, O-C_1-C_4-alkyl and phenyl, and where the phenyl ring may also carry one or two of the following radicals: chlorine, bromine, fluorine, branched and unbranched C_1-C_4-alkyl,

nitro, amino, C_1-C_4-alkylamino, C_1-C_4-dialkylamino, OH, O-C_1-C_4-alkyl, CN, SO_2-C_1-C_4-alkyl.

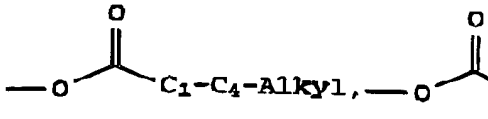
Please amend claim 8 as follows:

8. (amended). A compound as claimed in claim 1, where R^3 is [-O-$(CH_2)_p$-G with p equal to 2, 3 or 4.] <u>$-D-(F^1)_p-(E)_q-(F^2)_r$-G where D is 0, F1 is a C_1-C_4 carbon chain, p is 1, q is 0 and r is 0.</u>


, $-SO_2R^{53}$, $-(C=N)-R^{53}$, $-CO-NHR^{53}$, $-(C=N)-NHR^{53}$,

worin

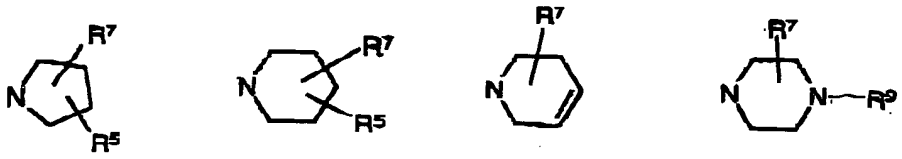
R^{53} verzweigtes oder unverzweigtes $O-C_1-C_6$-Alkyl, Phenyl, verzweigtes oder unverzweigtes C_1-C_4-Alkyl-Phenyl, wobei bei R^{52} und R^{53} unabhängig voneinander ein Wasserstoff des C_1-C_6-Alkylrests durch einen der folgenden Reste substituiert sein kann: OH, $O-C_1-C_4$-Alkyl, Cyclohexyl, Cyclopentyl, Tetrahydronaphthyl, Cyclopropyl, Cyclobutyl, Cycloheptyl, Naphthyl und Phenyl, wobei die Carbocyclen der Reste R^{52} und R^{53} unabhängig voneinander noch einen oder zwei der folgenden Reste tragen können: verzweigtes oder unverzweigtes C_1-C_6-Alkyl, verzweigtes oder unverzweigtes $O-C_1-C_4$-Alkyl, OH, F, Cl, Br, J, CF_3, NO_2, NH_2, CN, COOH, $COOC_1-C_4$-Alkyl, C_1-C_4-Alkylamino, CCl_3, C_1-C_4-Dialkylamino, $SO_2-C_1-C_4$-Alkyl, SO_2Phenyl, $CONH_2$, $CONH-C_1-C_4$-Alkyl, CONHPhenyl, $CONH-C_1-C_4$-Alkyl-Phenyl, $NHSO_2-C_1-C_4$-Alkyl, $NHSO_2$Phenyl, $S-C_1-C_4$-Alkyl,

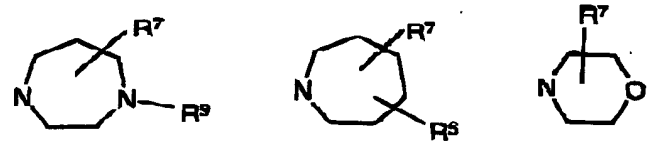


CHO, $CH_2-O-C_1-C_4$-Alkyl, $-CH_2O-C_1-C_4$-Alkyl-Phenyl, $-CH_2OH$, $-SO-C_1-C_4$-Alkyl, $-SO-C_1-C_4$-Alkyl-Phenyl, $-SO_2NH_2$, $-SO_2NH-C_1-C_4$-Alkyl

und zwei Reste eine Brücke $-O-(CH_2)_{1,2}-O-$ bilden, bedeuten kann,

B





sein kann und